AF

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/922,568 | 08/03/2001 | Udo Baron | TTV-088CPADV2 | 9670 |

22428 7590 10/31/2005

FOLEY AND LARDNER LLP
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

| EXAMINER | |
|---|---|
| QIAN, CELINE X | |
| **ART UNIT** | **PAPER NUMBER** |
| 1636 | |

DATE MAILED: 10/31/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/922,568 | BARON ET AL. | |
| | Examiner | Art Unit | |
| | Celine X. Qian Ph.D. | 1636 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *19 August 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *32-50,55 and 56* is/are pending in the application.

4a) Of the above claim(s) *33-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32,40-50,55 and 56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 August 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

Claims 32-50, 55 and 56 are pending in the specification. Claims 33-39 are withdrawn from consideration for being directed to non-elected subject matter. Claims 32, 40-50, 55 and 56 are currently under examination.

This Office Action is in response to the Amendment filed on 8/19/05.

### *Response to Amendment*

The rejection of claims 32, 40-50, 55 and 56 under 35 U.S.C.101/112 1st paragraph has been withdrawn in light of Applicant's arguments.

The rejection of claims 32, 40-50, 55 and 56 under 35 U.S.C. 112 1st paragraph is maintained for reasons set forth of the record mailed on 12/9/04 and further discussed below.

### *Response to Arguments*

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 32, 40-50, 55 and 56 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In response to this rejection, Applicants argue that the claims do not require the transgenic animal to have a phenotype, only expression of the gene of interest at detectable levels. Applicants assert that one of skill in the art would know how to use the claimed

transgenic animal such as producing a therapeutic protein. Applicants further assert that the specification provides extensive guidance on how to prepare a transgenic animal as claimed, including how to make the fusion proteins and how to make the transgenic animals (page 10-16 and 28-37). Furthermore, Applicants assert that the prior art demonstrates that one of skilled in the art could make the claimed invention without undue experimentation. Applicants argue that positional effects would not render the claimed invention unpredictable because it can be identified by routine screen which is not undue experimentation. Moreover, Applicants reiterates the arguments based on references cited previously, and argues that these references demonstrate the routine production of transgenic animals comprising gene expression systems resulting in detectable expression of gene of interest. Applicants further submit Schultz et al., St. Onge et al., Kistner et al. and Weinmann et al. to demonstrate that production of higher transgenic mammalian organisms, such as mice, using systems similar to the claimed invention is routine. Further, Applicants argue that the examiner fails to provide evidence to explain why one of skilled in the art cannot activate an endogenous gene. Applicants submit a representative list of references demonstrating the regulation of endogenous genes. Applicants thus conclude that the claimed invention is enabled by the instant specification.

The above arguments have been fully considered but deemed unpersuasive. The reasons for non-enablement of the claimed invention were discussed in detail in the previous office actions. Applicants apparently misconstrue the meaning of the phenotype in the context of the claimed invention. As clearly set forth in the previous office action, the phenotype does not necessary mean a specific diseased symptom, but rather the feature the transgenic animal displays as the result of the integration of the transgene such that distinguishes it from a normal

animal. In the instance wherein the transgenic animal is used to produce a therapeutic protein, such phenotype is production of the therapeutic protein by said transgenic animal. However, as discussed in the previous office action, the state of art at the time of filing regard producing transgenic animal with a specific phenotype as unpredictable (for example, see page 4 and 5 of the office action mailed on 7/15/03, and page 5-6 of the office action mailed on 12/9/04). The specification does not teach how to overcome the art-recognized unpredictability and make the claimed transgenic animal comprising the transgene that activates the transcription of a gene of interest at detectable level. The specification on page 10-16 only teaches the generation of the fusion construct cites prior art that teaches general method of making some transgenic animals. The specification on page 28-37 demonstrates the expression of the fusion protein *in vitro* cell culture, not in any transgenic animal system. As such, the specification does not teach how to overcome the art-recognized unpredictability and make the claimed transgenic animal comprising the transgene that activates the transcription of a gene of interest at detectable level. The examiner does not agree that the unpredictability in the art of making transgenic animals such as positional effect can be overcome by routine experimentation. Even if one transgenic system such as mouse can be produced, it does not extend the predictability to other transgenic animals.

In response to Applicants' arguments based on art cited in the previous office action, the examiner maintains the position that these references fail to provide enablement for the instantly claimed transgenic animals for same reasons as set forth in the previous office action (see page 6-8). Contrary to Applicants' assertion, the instantly cited references Schultz et al., St. Onge et al., Kistner et al. and Weinmann et al. do not demonstrate that production of higher transgenic

mammalian organisms, such as mice, using systems similar to the claimed invention is routine. The examiner would like to point out that Weinmann et al. is directed to the generation of a transgenic plant, which cannot be relied on for the enablement of a transgenic non-human animal. Further, the generation of the transgenic mouse system discussed in Schultz et al., St. Onge et al. and Kistner et al. is result from trial and error, not routine experimentation. Moreover, as discussed in the previous office action and above, the successful generation of a mouse system does not extend the predictability to other non-human animals.

Lastly, the examiner clarifies that the statement of "the transcriptional regulatory systems taught by Angeletti et al., Shigehara et al., Hasan et al. are limited to regulating exogenous reporter gene system" does not mean that endogenous genes cannot be regulated by a transcriptional regulatory system. Rather, it means that these references all demonstrate the regulation of a reporter gene system that is inserted into the genome. As asserted by Applicants, St. Onge also demonstrates the activation of an exogenous gene system, not an endogenous gene. A review of the references provided in exhibit E does not yield any teaching with regard to the instantly claimed transgenic animal system. Applicants are invited point out which reference and specific teaching in that reference provides support for the activation of an endogenous gene in the claimed transgenic animal system.

In view of the unpredictability of the generation of a transgenic animal with predictable phenotype, one skilled in the art would have to engage in undue experimentation to make and use the claimed invention because the instant specification fails to provide teaching that would overcome such unpredictability. Therefore, this rejection is maintained.

***Conclusion***

No claims are allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

This application contains claims 33-39 drawn to an invention nonelected with traverse in the response filed on 4/25/03. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X. Qian Ph.D. whose telephone number is 571-272-0777. The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Celine X Qian Ph.D.
Examiner
Art Unit 1636

CELIAN QIAN
PATENT EXAMINER